

REMARKS

Claims 1 and 4 – 12 have been cancelled without prejudice.¹

Claim 2 has been amended to recite “[a] biological process for producing carotenoids ‘including astaxanthin, the process’ comprising...”. Conforming amendments reciting carotenoids “including astaxanthin” are also provided. Claim 2 has also been amended to recite at the end of the claim, “wherein the astaxanthin content of the isolated carotenoids is greater than that which results from cultivating in the absence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate.” Support is found in the Specification, for example, at page 2, lines 9-10; and Example 2 at Page 6, line 6 to Page 7, line 18.

Claims 13 and 15 have been amended to delete the Markush language “selected from the group consisting of”, the singular “a” has been added prior to recitation of -- squalene synthase inhibitors -- in claim 13 and prior to recitation of -- phenoxypropylamine-type squalene synthase inhibitors -- in claim 15, and the plural “inhibitors” has been replaced with -- inhibitor -- in both claims.

Claims 2 and 13 are also amended to correct obvious errors by replacing the preposition “for” with -- of --.

Because claim 14 has been withdrawn, the dependency of claim 15 has been revised from that of claim 14 to that of claim 13. To insure that antecedent support with respect to the amended claim dependency is proper, claim 15 has been

¹ Withdrawn claim 5 is included among the presently cancelled claims.

amended to delete "ammonium ion based" which modified -- squalene synthase inhibitor --.

Claims 18 and 19 have been amended to more closely conform with U.S. practice. The amendments do not change the scope of the claims.

It is requested that upon finding the claims allowable with regard to the elected species, the Examiner continue to search non-elected species of inhibitors of biosynthesis of sterols from farnesyl pyrophosphate.

Indefiniteness Rejection

Claims 1-4, 6-13, and 15-21 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for three reasons. (Paper No. 20071109 at 2.)

In making the first rejection, the Examiner asserted that "[c]laims 13 and 15 are confusing in the recitation of a Markush group devoid of a listing of members." (Id.)

In making the second rejection, the Examiner asserted that "[c]laims 9-10 and 18-19 are confusing in that applicant fails to set forth the criteria that define a "concentration of the said inhibitor" other than providing, a functional definition of "inhibitor" as "giving less than ... reduction of the cell growth" of undefined microorganisms using undefined inhibitors." (Id.) The Examiner contended that "[s]uch functional language describes nothing about the chemical, physical or structural properties of these microorganisms, the compounds used or their concentration." (Id.)

In making the third rejection, the Examiner asserted that "[t]he claims are incomplete in the absence of a recovery step for the product produced." (Id. at 3.) With

respect to this rejection, the Examiner acknowledged that "there is no specific rule or statutory requirement which specifically addresses the need for a recovery step in a process of preparing a composition . . .". (Id.)

Initially, we note that claims 1 and 4-12 have been cancelled without prejudice. Accordingly, the rejections of those claims have been rendered moot and should be withdrawn.

With respect to the first rejection, in an effort to further prosecution, the Markush language has been deleted from claims 13 and 15. Accordingly, this rejection has been rendered moot and should be withdrawn.

With regard to the second rejection, we note that "[i]n rejecting a claim under the second paragraph of section 112, ***it is incumbent on the Examiner to establish that one having ordinary skill in the art would not have been able to*** ascertain the scope of protection defined by the claim when read in light of the supporting specification." *Ex parte Cordova*, 10 USPQ2d 1949, 1952 (Board of Pat. App. and Int. 1989), citing *In re Moore*, 169 USPQ 236 (CCPA 1971).

We respectfully submit that one skilled in the art would be apprised of the meaning of claims 18 and 19 in light of the Specification. For example, on page 4, lines 26-31 of the Specification discloses the addition of an inhibitor of sterol biosynthesis from FPP to the medium in the range of concentrations as recited in claims 18 and 19. One skilled in the art may also refer to Example 1 of the specification, entitled "Effect of addition of the squalene synthase inhibitor on the cell growth of *Phaffia rhodozyma*", from Page 5, line 21 to Page 6, line 5, which discloses representative ranges of inhibitor

and effect on cell growth. In view of this disclosure, we submit that claims 18 and 19 comply with § 112, second paragraph.

The Examiner also appears to express concern over the fact that various process parameters, e.g., “undefined microorganisms using undefined inhibitors”, are not recited in the claims. (Paper No. 20071109 at 2). The legal standard for definiteness, however, is whether a claim reasonably apprises those of skill in the art of its scope. *In re Warmerdam*, 31 USPQ 2d 1754, 1759 (Fed. Cir. 1994). Here, the amended claims meet that standard by explicitly reciting “a microorganism which is capable of producing carotenoids and belonging to the genus *Xanthophyllomyces (Phaffia)*”. Also, squalene synthase inhibitors are disclosed in the Specification and are known in the art, as indicated on Page 3, lines 14-16, and numerous examples of squalene synthase inhibitors are provided, e.g., from Page 3, line 24 – Page 4, line 12. The claims appraise **what** the invention is, and 35 USC § 112, second paragraph, does not require that the claims recite every detail of **how** it can or should be done.

In addition, we respectfully submit that the Examiner has made an unsubstantiated claim regarding (the first) point of novelty. As will be shown in the various arguments presented herein, amended claim 2 upon which claims 18 and 19 ultimately depend, is entitled to allowance. For each of the foregoing reasons, the rejection as to pending claims 18 and 19 should be withdrawn.

With regard to the third rejection (i.e., that a recovery step should be recited), claim 1 has been cancelled without prejudice. Accordingly, this rejection has been rendered moot.

In sum, it is submitted that the present claims fully satisfy 35 USC 112, second paragraph. Withdrawal of all indefiniteness rejections is respectfully requested.

35 USC § 112, First Paragraph Rejection

Claim 3 was rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." (Paper No. 20071109 at 3.) In making the rejection, the Examiner asserted that "[t]he invention appears to employ a specific strain of *Xanthophyllomyces*. It is not clear if the written description is sufficiently repeatable to avoid the need for a deposit. Further it is unclear if the starting materials were readily available to the public at the time of invention." (Id.)

The Examiner also asserted that "[i]t appears that a deposit was made in this application as filed as noted on page 3 of the specification. However, it is not clear if the deposit meets all of the criteria set forth in 37 CFR 1.801-1.809." (Id. at 4.) The Examiner stated that "[a]pplicant or applicant's representative may provide assurance of compliance with the requirements of 35 U.S.C § 112, first paragraph."

Additionally, the Examiner asserted that the "deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository and the complete taxonomic description." (Id. at 5.)

Although we disagree with the Examiner's position, with a view toward furthering prosecution, the following is provided upon information and belief: a strain of *Xanthophyllomyces* (*Phaffia*) according to the present invention was originally deposited

with the American Type Culture Collection (ATCC) (located at 10801 University Blvd., Manassas, VA 20110-2209). The strain was assigned accession no. ATCC96594. Subsequently, the strain was redeposited with the ATCC on April 8, 1988 pursuant to the Budapest treaty on April 8, 1998. All restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot.

Regarding the Examiner's requirement to reference the deposit in the body of the Specification, it is submitted that the required information is already provided in the Specification from page 2, line 34 to page 3, line 6. Thus, no additional information is believed to be required.

In sum, we respectfully submit that the rejection has been rendered moot. Withdrawn of the rejection is requested.

Anticipation Rejections

A. Muramatsu

Claims 1, 4, and 9-12 were rejected under 35 U.S.C. § 102(e) as being anticipated by Muramatsu et al. (U.S. Patent No. 6,972,191) ("Muramatsu"). (Id. at 5.)

With a view toward furthering prosecution, claims 1, 4 and 9-12 have been cancelled, without prejudice. Accordingly, the rejection has been rendered moot and should be withdrawn.

B. An

Claims 1-2, 4, 9-14, and 18-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by An et al. (Applied and Environmental Microbiology, Jan. 1989, Vol. 51, p. 116-124) ("An"). (Paper No. 20071109 at 5.)

An discloses "[i]solation of *Phaffia rhodozyma* [m]utants with [i]ncreased [a]staxanthin [c]ontent". (Title.) An further discloses that "astaxanthin-producing yeast *Phaffia rhodozyma* [plated with] antimycin A gave rise to colonies of unusual morphology, [and] "[o]ne of the antimycin strains (ant-1) and a ... derivative of ant-1 ... produced considerably more astaxanthin than the parent...". (Abstract, lines 1-7.) It appears that the Abstract and Discussion sections of the An disclosure are directed entirely to discussion of the results obtained with the antimycin-A and antimycin derivative strains.

An also discloses other ways of "[trying] to develop selection procedures for astaxanthin overproduction." (Page 118, right col., 17th and 16th lines from the bottom.) In one approach, An "tried to develop [such] selection procedures [by selecting] for resistance to 2-deoxyglucose....". (Page 117, right col., 8th line from the bottom to Page 118, left col., line 5; and Page 118, right col., 19th to 15th line from the bottom.) An discloses that this "was not successful in isolating highly pigmented mutants." (Page 118, right col., 17th and 14th lines from the bottom.)

Pertaining to another approach, An discloses that "[s]everal inhibitors of sterol biosynthesis ... or carotenoid biosynthesis were incorporated in YM agar, and **resistant colonies were evaluated for astaxanthin production**....Concentrations that gave [greater than or equal to] 90% kill were determined, and then 30 to 100 YM agar

plates containing the inhibitors were inoculated with sufficient cells to give 100 to 500 surviving colonies. Colonies were visually screened for color changes.” (Page 118, left col., lines 6-15) (emphasis added.) An discloses that *P. rhodozyma* strains resistant to sterol biosynthesis inhibitors ... **did not yield high-producing strains**. Several of the inhibitors tested ...changed the color of the colonies distinctly, indicating a change in carotenoid composition. However, **since the visual appearance or absorbance spectra of extracts did not resemble astaxanthin, we did not analyze the carotenoids produced in the presence of the inhibitors.**” (Page 118, right col., 8th line from the bottom to Page 119, left col., line 2) (emphasis added.)

In making the rejection, the Examiner asserted that “[An] teaches a method of culturing strains of *Xanthophyllomyces(Phaffia)* that is capable of producing carotenoids in the presence of an inhibitor of squalene synthase inhibitor. See, e.g., page 118, paragraph 2.” (Id. at 6.)

As is well settled, anticipation requires “identity of invention.” *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply*, 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir 1984).

Furthermore, in a §102(b) rejection there must be no difference between what is claimed and what is disclosed in the applied reference. *In re Kalm*, 154 USPQ 10, 12 (CCPA 1967); *Scripps v. Genentech Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). “Moreover, it is incumbent upon the Examiner to **identify wherein each**

and every facet of the claimed invention is disclosed in the applied reference.” *Ex parte Levy*, 17 USPQ2d 1461, 1462 (BPAI 1990). The Examiner is required to point to the disclosure in the reference “**by page and line**” upon which the claim allegedly reads. *Chiong v. Roland*, 17 USPQ2d 1541, 1543 (BPAI 1990).

Initially, we note that with a view towards furthering prosecution, claim 1 has been cancelled and claim 2 has been amended. Amended claim 2 recites “[a] biological process for producing carotenoids including astaxanthin, the process comprising cultivating a microorganism which is capable of producing carotenoids including astaxanthin and belonging to the genus *Xanthophyllomyces (Phaffia)* in the presence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate, a substrate for producing carotenoids including astaxanthin, in an aqueous nutrient medium under aerobic conditions, and isolating the resulting carotenoids including astaxanthin, from the cells of said microorganism or from the cultured broth, wherein the astaxanthin content of the isolated carotenoids is greater than that which results from cultivating in the absence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate.”

In view of the foregoing, we submit that An lacks “identity of invention” with the amended claims of the present application, which are currently pending and under examination. An discloses that only [strains] resistant [to sterol biosynthesis inhibitors] were evaluated for astaxanthin production. (Page 118, left col., lines 6-8; and right col., 8th to 6th line from the bottom.) Thus, An only extracted carotenoids from *resistant* colonies. (Page 118, left col., line 6 to right col., line 4.) The present claims, on the other hand, do not recite a limitation of screening for strains resistant to sterol

biosynthesis inhibitors and/or isolating carotenoids from the cells of such (resistant) microorganism or from the cultured broth of such (resistant) strain. Stated another way, An does not disclose the scope of the presently claimed "biological process for producing carotenoids including astaxanthin, the process comprising cultivating a microorganism which is capable of producing carotenoids including astaxanthin and belonging to the genus *Xanthophyllomyces (Phaffia)* in the presence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate, a substrate for producing carotenoids including astaxanthin, in an aqueous nutrient medium under aerobic conditions, and isolating the resulting carotenoids including astaxanthin, from the cells of said microorganism or from the cultured broth...". For this reason alone, the rejection should be withdrawn.

In addition, An does not disclose each and every element of amended claim 2. As indicated above, An discloses that the "*P. rhodozyma* strains resistant to sterol biosynthesis inhibitors ... did not yield high producing strains." (Page 118, right col., 8th to 6th line from the bottom.) An further discloses that "since the visual appearance or absorbance spectra of extracts did not resemble astaxanthin, we did not analyze the carotenoids produced in the presence of the inhibitors." (Page 118, right col., 8th line from the bottom to Page 119, left col., line 2.) For a scientific paper that explicitly set out to identify "...[m]utants with [i]ncreased [a]staxanthin [c]ontent" (Title), An apparently indicates that the visual appearance with regard to astaxanthin was such that analysis of the carotenoids was not even worth undertaking. One skilled in the art would understand the An disclosure as indicating that little or no astaxanthin was produced by the resistant strains, and that, in any event, the strains were not mutants

with increased astaxanthin content. Thus, An lacks disclosure of the claimed process for producing carotenoids in which astaxanthin content of carotenoids isolated from *Xanthophyllomyces (Phaffia)* cultivated in the presence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate, is greater than that which results from cultivating in the absence of such an inhibitor. For this additional reason, the rejection has been rendered moot.

Reconsideration and withdrawal of the rejection are requested.

Obviousness Rejection

Claims 1-4, 6-13 and 15-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over An in view of Brown et al. (Brown, G.R., et al., "Phenoxypropylamines: A New Series of Squalene Synthase Inhibitors," J. Med. Chem., vol. 38, no. 21, pp. 4157-4160 (1995) ("Brown") is of record.) (Paper No. 20071109 at 6.)

An is summarized above.

Brown discloses that "phenoxypropylamines ... represent a ... series of orally active [squalene synthase] SQS inhibitors." (Page 4157, left col., lines 23-25.) Brown discloses structure-activity relationships upon "seeking a ... series of SQS inhibitors with [desired properties]." (Page 4157, left col., lines 24-31; and Brown in entirety.)

In making the rejection, the Examiner asserted that "[An] discloses a method of culturing strains of *Xanthophyllomyces (Phaffia)* that is capable of producing carotenoids in the presence of an inhibitor of squalene synthase. See, e.g., page 118, paragraph 2." (Id.) The Examiner acknowledged that "[An] differs from the claimed

invention in that the inhibitor of squalene synthase is not a phenoxypropylamine compound and is not specifically [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine.” (Id.)

To fill the acknowledged gap, the Examiner asserted that [Brown] adequately demonstrate[s] that this phenoxypropylamine compound is known in the art as a squalene synthase inhibitor.” (Id. at 6.)

The Examiner then concluded that “it would have been obvious to ... modify the process of [An] by culturing *Xanthophyllomyces (Phaffia)* for the production of a variety of carotenoids using a different inhibitor of squalene synthase ... such as the phenoxypropylamine compound [3-(3-allylbiphenyl-4-yloxy)-propyl]-isopropyl-amine for the expected benefit of maximizing the yield of the ... carotenoids useful as food additives and in pharmaceutical applications.” (Id.) The Examiner further concluded that “the claimed invention as a whole was . . . *prima facie* obvious, especially in the absence of evidence to the contrary.” (Id.)

It is well settled the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and modify the document(s) relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v.*

Teleflex Inc., 127 S.Ct. 1727, 1731-32 (2007) (the obviousness “**analysis should be made explicit**” and the teaching-suggestion-motivation test is “**a helpful insight**” for determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to modify document(s) must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion test should “**be based on objective evidence of record**.” *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added). See also *Examination Guidelines for Determining Obviousness*, 72 Fed. Reg. 57526, 57528 (October 10, 2007) (“The key to supporting any rejection under 35 USC § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.”).

Respectfully, we submit that the rejection is devoid of a proper § 103 analysis in support of the proposed modification and combination. All that is there are conclusory statements such as the assertion that “it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of [An] by culturing *Xanthophyllomyces (Phaffia)* for the production of a variety of carotenoids using a different inhibitor of squalene synthase ... such as the phenoxypropylamine compound [3-(3-allylbiphenyl-4-yloxy)-propyl]-isopropyl-amine for the expected benefit of maximizing the yield of the ... carotenoids useful as food additives and in pharmaceutical applications.” (Paper No. 20071109 at 6.)

Here, what the rejection should have done, but did not, was to explain on the record **why** one skilled in this art would modify the disclosure of An and combine An with Brown in the manner proposed by the Examiner to arrive at the claimed process.

As is well settled, an Examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done. *Takeda Chem. Indus., Ltd v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. June 28, 2007) (citing *KSR*) (indicating that "it remains necessary to identify **some reason** that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound") (emphasis added); *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). But this is precisely what the Examiner has done here. Thus, the rejection is legally deficient and should be withdrawn for this reason alone.

Notwithstanding the legally insufficient nature of the rejection, we note that the rejection is also factually insufficient to support a rejection under § 103(a). In doing so we observe that obviousness cannot be based upon speculation, nor can obviousness be based upon possibilities or probabilities. Obviousness **must** be based upon facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (CCPA 1970). When a conclusion of obviousness is not based upon facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (BPAI 1993). Further, "to establish *prima facie* obviousness of a claimed invention, **all claim limitations must be taught or suggested by the prior art.**" MPEP § 2143.03 (citing *In re Royka*, 180 USPQ 580 (CCPA 1974)) (emphasis added).

First, as indicated above in response to the rejection under 35 USC § 102 based on An, there are factual gaps in the Examiner's assertions regarding An. We

hereby incorporate the arguments made above in response to the 35 USC § 102 rejection over An.

Brown does not even come close to filling the deficiencies of An. Brown merely discloses that “the phenoxypropylamine compound is known in the art as a squalene synthase inhibitor”, as alleged by the Examiner (Paper No. 20071109 at 6.) Brown provides no disclosure, however, of the use of a phenoxypropylamine compound, however, to culture *Xanthophyllomyces (Phaffia)* and produce carotenoids. In short, the rejection identifies no disclosure in Brown that would fill the gaps in An. For this reason as well the rejection should be withdrawn.

Moreover, we disagree with the Examiner’s unsupported assertion that the combination of An and Brown is somehow “for the expected benefit of maximizing the yield of the ... carotenoids useful as food additives and in pharmaceutical applications.” (Paper No. 20071109 at 6.) Based on the disclosure of An, whether alone or in combination with Brown, one skilled in the art would not ascertain such an “expected benefit” as alleged by the Examiner. In fact, as noted above An discloses that the “*P. rhodozyma* strains resistant to sterol biosynthesis inhibitors ... **did not yield high producing strains.**” (Page 118, right col., 8th to 6th line from the bottom.) An further discloses that “**since the visual appearance or absorbance spectra of extracts did not resemble astaxanthin, we did not analyze the carotenoids produced in the presence of the inhibitors.**” (Page 118, right col., 8th line from the bottom to Page 119, left col., line 2.) As noted above, for a scientific paper that explicitly set out to identify “...[m]utants with [i]ncreased [a]staxanthin [c]ontent” (Title), An apparently indicates that the visual appearance with regard to astaxanthin was such that analysis

of the carotenoids was not even worth undertaking. Thus, one skilled in the art would understand An as indicating that little or no astaxanthin was produced by the resistant strains, and that, in any event, the strains were not mutants with increased astaxanthin content. The Examiner has not indicated where in such a disclosure the alleged "expected benefit" can be found. It is submitted that, contrary to the Examiner's assertion, one skilled in the art would not derive an expectation of success from the disclosure of An, whether alone or in combination with Brown.

Beyond looking at the cited documents to determine if any of them suggests doing what the inventors have done, one must also consider if the art provides the required expectation of succeeding in that endeavor. See *In re Dow Chem. Co. v. American Cyanamid Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) ("Both the suggestion and the expectation of success must be founded in the prior art, not in applicants' disclosure.") "Obviousness does not require absolute predictability, but a reasonable expectation of success is necessary." *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976). Furthermore, the U.S. Patent and Trademark Office Examination Guidelines at page 57527 provide the following guidance to Examiners: "In short, the focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge". However, no such motivation or expectation of success can be found in the cited documents, as indicated above.

In view of An's disclosure from which one skilled in the art would not expect success in the presently claimed process, An fails to teach, suggest, or motivate

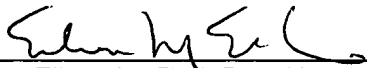
one skilled in the art to achieve the claimed biological process for producing carotenoids in which the astaxanthin content of carotenoids isolated from *Xanthophyllomyces* (*Phaffia*) cultivated in the presence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate, is greater than that which results from cultivating in the absence of such an inhibitor. More fundamentally, An leads one skilled in the art away from the process as presently claimed. As is well settled, to do what the prior art teaches against is the very antithesis of obviousness. See, e.g., *In re Rosenberger*, 156 USPQ 24, 26, (CCPA 1968) and *In re Buehler*, 185 USPQ 781, 787 (CCPA 1975). For this reason also, the rejection should be withdrawn.

Contrary to An which leads away from the claimed process, it has been found that in accordance with the claimed process, “[a]staxanthin production was enhanced in all conditions tested.” (Specification, Page 7, line 16.) Example 2 of the present application discloses the “[e]ffect of addition of the squalene synthase inhibitor on the astaxanthin production by *Phaffia rhodozyma*”. (Example 2 heading on Page 6, lines 6-7; and Example 2 from Page 6, line 6 to Page 7, line 18.) Table 2 on Page 7 includes data showing that “[a]staxanthin production was enhanced” at all concentrations of [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine used as compared to cultivation without the inhibitor. Also, the data indicates that “[a]staxanthin production was enhanced” upon each increased concentration of inhibitor tested. The improved results disclosed are unexpected in view of the disclosure of An.

For each of the foregoing reasons, it is submitted that the rejection has been rendered moot. Withdrawal of the rejection is requested.

Accordingly, for the reasons set forth above, withdrawal of the rejections and allowance of the claims are respectfully requested. If the Examiner has any questions about this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop Amendment, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 29, 2008.



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